REMARKS

Claims 36 to 39 and 42 to 50 were pending in the application before entry of the present amendment. Claims 36 to 39 are withdrawn from consideration. Claim 49 has been canceled without prejudice. Applicants reserve their right to prosecute the subject matter of claim 49 in one or more continuation-in-part, continuation, or divisional applications. Claim 45 has been amended to incorporate the limitations of claim 49. Support for the amendment can be found in the specification as filed, *e.g.*, at page 87, lines 19 to 22.

Claims 43 and 48 have been amended to correct a clerical error; due to the lack of antecedent basis for "stop codon," the definite article in original claims 43 and 48, respectively, has been changed to an indefinite article.

Claim 42 has been amended to more clearly point out what Applicants consider the invention. Support for the amendment to claim 42 can be found in the specification as filed at page 90, line 14 to page 91, line 25.

Claims 42 to 46 have been amended to recite that the claimed virus particle is a live-attenuated virus. Support for the amendment can be found in the specification as originally filed at page 13, lines 25 to 28.

THE REJECTIONS UNDER 35 U.S.C. § 101 SHOULD BE WITHDRAWN

Claims 42, 43, and 45 to 49 are rejected under 35 U.S.C. § 101 allegedly for lack of utility. Specifically, the claims have been rejected because the claims allegedly read on inoperable species.

First, claims 42 to 46 have been amended to clarify that the isolated and attenuated virus particle is a live virus particle. Second, the claims recite that "the virus exhibits a lower degree of virulence as compared to a wild type RSV." At page 15, lines 12 to 15, of the specification as originally filed, it is stated that such live-attenuated virus particles have utility as anti-RSV vaccines. The claims do not cover a virus without any virulence. Thus, the virus particles of the claimed invention can be used as immunogenic compositions or as anti-RSV vaccines.

Further, claim 42 has been amended to recite that the truncation is less than 46 amino acids in length. The operability of a truncation of less than 46 amino acids has been demonstrated in Section 12.2 starting at page 90, line 13. Accordingly, claim 43 has been amended to delete all stop codons that would result in truncations longer than 45 amino acids.

Claims 47 and 48 depend from claims 45 and 46, respectively. Thus, the above-made arguments relating to claims 42 to 46 apply equally to claims 47 and 48.

Claim 49 has been canceled. The rejection of claim 49 is therefore moot.

According to the Utility Examination Guidelines, Federal Register Vol. 66, No. 4, January 5, 2001,

> [a]n invention has a well-established utility (1) if a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (*e.g.*, properties or applications of a product or process), and (2) the utility is specific, substantial, and credible.

The utility guidelines further state that a rejection should not be imposed "if the applicant has asserted that the claimed invention is useful for any particular practical purpose [. . .] and the assertion would be considered credible by a person of ordinary skill in the art."

In the specification as filed, *e.g.*, at page 15, lines 12 to 15, it is stated that the claimed viral particles can be used, among others, as expression vectors or as live attenuated anti-RSV vaccines. The particular practical purpose of using the claimed compositions as anti-RSV vaccines is, *e.g.*, to protect a subject from RSV. That attenuated live viruses can be used as vaccines is an established concept. The successful application of attenuated RSV as vaccines has for example been shown in Jin *et al.*, 2003, Vaccine 21:3647-3652. Thus, Applicants have demonstrated the utility of the claimed compositions because the asserted use is specific, substantial, and credible.

Claims 45 to 49 are further rejected under 35 U.S.C. § 101 because claim 45 reads on viruses whose Cys3His motif is not maintained. Solely in an effort to expedite prosecution and without making any admissions as to the merits of this rejection, Applicants have amended claim 45 to incorporate the limitations of claim 49. In view of this amendment, the rejection should be withdrawn.

In view of the foregoing, Applicants submit that the rejection under 35 U.S.C. § 101 has been obviated and should be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN

Claims 42 and 43 were rejected under section 112, first paragraph, of Title 35 of the United States Code allegedly for lack of enabling support in the specification. In particular, the Examiner contends that the scope of the claim is not enabled because Applicants have

allegedly not demonstrated that any truncation is likely to result in operable inventions. Applicants respectfully contend that the full scope of the claims as amended is enabled.

Claim 42 has been amended to recite that the truncation "is less than 46 amino acids in length." The first stop codon using the primer MSCH 3 begins at nucleotide position 8137 and generates a truncation of 17 amino acids (page 91, line 18). The next truncation was created using the primer MSCH 2 whose first stop codon begins at nucleotide position 8050. The difference between MSCH2 and MSCH3 results in a further shortening of the M2-1 protein by 29 amino acids. Thus, a truncation generated with primer MSCH2 is 46 amino acids in length (29 amino acids plus 17 amino acids). The virus with the truncation of M2-1 by 17 amino acids has been shown to be virulent and a replication rate 15-fold less than the replication rate of wild type RSV in the lung of cotton rats has been demonstrated (see, *e.g.*, the specification as filed, at page 91, lines 23 to 26), whereas RSV with a deletion of more than 45 amino acids in M2-1 could not be recovered. Accordingly, claim 43 has been amended to delete all stop codons that would result in truncations of more than 45 amino acids in length.

Applicants have shown how to make and use a truncation of 17 amino acids. Tang *et al.*, 2001, Journal of Virology 75:11328-11335 ("Tang;" cited by the Examiner in the Office action) shows that deletions of 46 or 67 amino acids did not result in the recovery of viable viruses. As the amended claim requires that the truncation is 45 amino acids or less, the remaining issue is whether truncations between 18 amino acids and 45 amino acids are enabled. The M.P.E.P. states in section 2164.02 that

> "lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement."

Therefore, the fact that no truncations of a length between 18 amino acids and 45 amino acids were actually generated and tested is not sufficient for a rejection under 35 U.S.C. § 112, first paragraph. Applicants submit that the description found in the specification as filed is adequate since it provides ample guidance for how to make and use the claimed respiratory syncytial virus that exhibits a lower degree of virulence as compared to a wild type virus. The specification as filed teaches that C-terminal deletions of the M2-1 protein can be introduced to generate an attenuated recombinant RSV, see, *e.g.*, the specification at page 15, line 20 and at page 87, lines 25 to 28. Examples for how such truncations can be introduced into the M2-1 protein are presented in section 12.2 (page 90, line 14 to page 91, line 26) of

the specification as filed. *E.g.*, the specification at section 6 (page 27, line 23 to page 30, line 5) provides teachings of how the recombinant virus can be rescued. Throughout the specification as filed, teachings can be found that relate to the determination of whether a recombinant RSV is attenuated. As described in the specification, an attenuated RSV is a virus that exhibits a lower degree of virulence as compared to a wild-type virus (the specification at page 20, lines 29 to 31). The virulence of a virus can be tested in various ways, *e.g.*, comparison of plaque morphology (the specification at page 63, lines 13-21) and growth kinetics (the specification at page 63, line 22 to page 64, line 8).

Further, Applicants respectfully point out that procedures for testing whether a viral particle is attenuated are routine in the art, and that the skilled artisan would be able to determine without undue experimentation which of the viral particles are covered by the pending claims. Thus screening procedures to test the viral particles of the invention an attenuated phenotype should not be considered undue experimentation since such procedures are well-known and routine to the skilled artisan. Applicants would like to direct the Examiner's attention to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)):

> " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.' "

Claim 44 has been rejected under 35 U.S.C. 112, first paragraph, for allegedly lacking enabling support in the specification. The Examiner argues that the scope of claim 44 is not enabled because the specification allegedly fails to provide sufficient guidance to determine which mutations in the M2-1 gene would result in the desired phenotype without undue experimentation. In particular, the Examiner argues that the claim reads on embodiments wherein the Histidine at position 25 of the protein is also mutated which would result in an inoperable species.

Applicants submit that the description found in the specification as filed is adequate since it provides ample guidance for how to make and use the claimed respiratory syncytial virus that exhibits a lower degree of virulence as compared to a wild type virus. The specification as filed teaches at page 87, lines 9 to 11, that different point mutations and lesions can be combined in a single virus to generate an attenuated recombinant RSV.

Examples for how such mutations can be introduced into the M2-1 protein are presented at page 21, line 1 to page 23, line 10 and in section 12 (page 87, line 1 to page 91, line 26) of the specification as filed. An exemplary teaching of how a recombinant virus can be rescued is provided in section 6 of the specification (page 27, line 23 to page 30, line 5). Throughout the specification as filed, teachings can be found that relate to the determination of whether a recombinant RSV is attenuated. As described in the specification, an attenuated RSV is a virus that exhibits a lower degree of virulence as compared to a wild-type virus (the specification at page 20, lines 29 to 31). The virulence of a virus can be tested in various ways, *e.g.*, comparison of plaque morphology (the specification at page 63, lines 13-21) and growth kinetics (the specification at page 63, line 22 to page 64, line 8). Thus, based on the guidance provided in the specification as filed and on the information known in the art, the skilled artisan can determine without undue experimentation which mutations that are introduced in the virus in addition to the mutation at position 96 result in a viable virus.

Claim 45 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. In particular, the claim 45 has been rejected because it reads on viruses in which the Cys3His motif is not maintained. In response, claim 45 has been amended to incorporate the limitation that the Cys3His motif is maintained. In view of the amendment, the rejection is moot.

Claims 42-50 are further rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the claims were rejected because the degree of virulence of the claimed virus was compared to the degree of virulence of "a wild type virus" without specification of the type of wild type virus. In response, Applicants have amended claim 42, 44, and 45 to recite that the virulence of the claimed virus is lower than the virulence of a wild type RSV. In view of the amendment, the rejection should be withdrawn.

Applicants assert that the instant specification in combination with information readily available to the skilled artisan at the time the instant application was filed fully enables the claimed invention and that the rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn.

CONCLUSION

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted, by Jacqueline Benn Reg No. 43,492

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Laura A. Coruzzi 30,742

Laura A. Coruzzi (Reg. No.)

JONES DAY
222 East 41st Street
New York, New York 10017
(212) 326-3939